Restoration of Regional Wall Motion by Nitroglycerin Therapy in Patients with Left Ventricular Asynergy*

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Abnormalities in regional wall motion are not uniformly improved following aortocoronary bypass operation. This study demonstrates that regional wall motion abnormalities may be reversed with nitroglycerin therapy. Eighteen asynergic regions in seven patients with coronary artery disease were studied before and after sublingually administered nitroglycerin. Although none of the normal areas became abnormal after nitroglycerin therapy, there were marked changes in the asynergic regions. Of the seven hypokinetic areas, three became normal. Of the 11 dyskinetic areas, 4 showed a normal reduction in area after nitroglycerin treatment. The study illustrates that because areas of regional dysfunction may not exist as fixed lesions, their recoverability can be realized by changing the loading conditions of the ventricle. Identification of such potentially viable areas of asynergy may prove helpful in the selection of cases for aortocoronary bypass operation.

Aortocoronary bypass operation has a variable effect on the function of the left ventricle.1-3 This may be due, in part, to inability to predict the behavior of regional wall abnormalities following revascularization. Areas of asynergy may have pronounced influence on left ventricular function,4,5 and yet traditional hemodynamic techniques measure the integrated response of the left ventricle as though all segments made a uniform contribution to total function. Previous investigations show that abnormal wall motion occurs in zones supplied by those arteries with critical stenosis.4,7

It is pertinent therefore to inquire whether these regional areas of malfunction are due to irreversibly damaged tissue or to viable but ischemic myocardial fibers, which under different loading conditions may be recruited in the contractile process. A demonstration that an asynergic segment supplied by an obstructed artery may be recoverable would help in case selection for bypass operation.

This study examines the question by quantitating regional wall motion before and after the administration of nitroglycerin (NTG) in patients with coronary artery disease.

METHODS

Seven patients undergoing diagnostic cardiac catheterization for anterior chest pain were selected for this study on the basis of their abnormal ventriculograms. They included six men and one woman and ranged in age from 46 to 60 years. Selective coronary arteriograms revealed occlusive disease in all cases. Each patient received premedication of 10 mg of diazepam orally. Through the right antecubital vein, a 7F Goodale-Lubin or Zucker bipolar pacing catheter was directed into the coronary sinus and advanced to the obtuse margin of the left ventricle. In this position, the catheter outlined the posterior arc of the atrioventricular groove. By continuous monitoring of phasic undamped coronary sinus pressure, care was taken to avoid wedging of the catheter. A transfemoral approach was used to pass a 100-cm multiple-hole catheter retrograde across the aortic valve and position it in the midleft ventricular cavity. After recording the heart rate and left ventricular pressures, a resting left ventricular angiogram was performed at 30° right anterior oblique, using 45 to 60 ml of meglumine diatrizoate (Renografin 76 percent) over 4 sec at 80 frames per sec. At least 15 min were allowed to elapse before the left ventricular end-diastolic pressure (LVEDP) either returned to levels before angiogram was performed or stabilized for another 5 min. At this juncture, 0.6 mg of nitroglycerin was administered sublingually. Five minutes following complete absorption of the pill (the time at which maximum decrease in left ventricular volume occurs)8-10 the heart rate and pressure were once again recorded, and a left ventricular angiogram repeated in a manner identical to that previously described.

Data Reduction and Analysis

The method for quantifying regional contraction patterns has been detailed in a previous report.6 The ventriculographic images selected for analysis were among the first four sinus-conducted beats following contrast injection. No postextrasystolic beats were analyzed. The left ventricle was visualized as a truncated ellipsoid of revolution subtended by the atrioventricular ring, which in turn (outlined by the coronary sinus catheter) served as an intracardiac plane of reference. The end-diastolic and end-systolic silhouettes were aligned and the junction of the aortic and mitral valves superimposed. The longitudinal axis, which was drawn only for end-diastole from apex to midpoint of the aortic valve, was quadrisected by six transverse chords, producing eight regional areas each (Fig 1) at end-diastole (D) and end-systole (S). Each regional area was integrated by an electronic planimeter in which output was plotted by a PDP 11/20 computer as the

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Table 2—Effect of Nitroglycerin on Regional Areas

<table>
<thead>
<tr>
<th></th>
<th>Before NTG</th>
<th>After NTG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>38</td>
<td>38</td>
</tr>
<tr>
<td>Hypokinetic</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Dyakinetic</td>
<td>11</td>
<td>4</td>
</tr>
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Regional Dynamics

Of the 56 regions examined, 38 had a normal systolic decrease in area prior to treatment with nitroglycerin (Table 2); that is, the fractional change in systolic dimensions was greater than 20 percent. None of these areas became abnormal following use of the nitrate. Of the seven hypokinetic areas, three contracted normally after NTG, two remained hypokinetic, and two became frankly dyskinetic. Of the 11 dyskinetic areas, 4 showed a normal reduction in area after therapy with the drug, 3 became hypokinetic, and 4 were unchanged. Therefore, 3 of 7 hypokinetic areas and 7 of 11 paroxysmic segments improved in their contraction pattern with administration of nitroglycerin. Eight of 18 abnormal segments either did not change or worsened with nitroglycerin treatment.

Figure 2 (A, B) illustrates one example of the effect of nitroglycerin therapy on regional wall motion in a patient with dyskinesis of the posterior wall. This does not represent the most dramatic amelioration of ventricular asynergy in the study, but it does demonstrate the reversibility of systolic expansion of a ventricular segment with use of nitroglycerin. The mitral valve prolapse indicated by the shaded area in Figure 2A was completely corrected in association with improvement in posterior wall motion.

Table 1—Effect of Nitroglycerin on Hemodynamics

<table>
<thead>
<tr>
<th>Patient, No.</th>
<th>Heart Rate</th>
<th>LVSP* (mm Hg)</th>
<th>LVEDP** (mm Hg)</th>
<th>EDV† (ml/m²)</th>
<th>EF‡†</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>C§</td>
<td>NTG</td>
<td>C</td>
<td>NTG</td>
</tr>
<tr>
<td>1</td>
<td>88</td>
<td>88</td>
<td>158</td>
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<td>6</td>
<td>71</td>
<td>79</td>
<td>124</td>
<td>130</td>
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<td>7</td>
<td>79</td>
<td>79</td>
<td>135</td>
<td>120</td>
<td>20</td>
</tr>
<tr>
<td>Mean</td>
<td>77</td>
<td>82</td>
<td>142</td>
<td>135</td>
<td>15</td>
</tr>
</tbody>
</table>

*Peak left ventricular systolic pressure.
**Left ventricular end-diastolic pressure.
†End-diastolic volume.
‡Ejection fraction.
§Control state.
†Nitroglycerin.

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the loading conditions of the ventricle. Distinct worsening of wall motion has been demonstrated following interventions such as atrial pacing and intravenously administered propranolol. In both cases, the mechanism was said to be due to an imbalance of the myocardial oxygen demand-to-supply ratio, which immobilized potentially viable ischemic tissue. In our investigation, most of the abnormal regions were improved with treatment with nitroglycerin, suggesting that an abnormal segment may be recoverable with a more favorable energy balance. This could imply that such an abnormal but potentially viable area may respond to the introduction of new blood supply by revascularization.

There are a variety of mechanisms by which nitroglycerin or a reduction in ventricular volume could affect regional wall motion. First, restoration of a normal contraction pattern in an asynergic area may occur by virtue of a reduction in wall tension. According to Laplace’s law, a decrease in ventricular volume without a corresponding change in intracavity pressure would decrease wall tension or wall stress, assuming no significant change in mural thickness. Such a decrease in tension on ischemic but viable muscle fibers would allow a greater capacity for fiber shortening. Second, nitroglycerin therapy may improve the contraction pattern of ischemic tissue by enhancing collateral blood supply with redistribution of blood flow through asynergic but viable zones of muscle. If this mechanism were operative, then improvement in contractile function and cardiac performance by revascularization would be all the more likely. Finally, improvement in contraction could occur because of the reflex catecholamine release, which may follow nitroglycerin administration. There is evidence, albeit sparse, to suggest that catechols can reverse segmental wall abnormalities.

In our series, 44 percent of the abnormal segments either remained the same or became frankly paradoxical following volume reduction with administration of nitroglycerin. One explanation for this occurrence is that a thin akinetic scar, although not possessing contractile properties, does have certain compliance characteristics. When studied experimentally, ischemic wall segments show significantly reduced compliance. After reduction of the total endocardial surface area of the ventricle, a shift in the passive length tension curve of the segment may take place, so that systolic expansion of a segment could appear during early force development. Another possible explanation for worsening of segmental kinetics is that nitroglycerin could influence the distribution of coronary flow in such a way that the ischemic one would be sacrificed in favor of perischemic and other contractile zones (the so-called coronary steal effect). Such an imbalance could result in more dyskinesis of the noncontractile segment. The cases in which no change in segmental motion occurred may indicate either a balance of opposing mechanisms or no discernible effect of the drug.

We defined hypokinesis as less than a 20-percent reduction in a regional systolic area. This is based on studies on normal ventriculograms in our laboratory, where there was greater than a 30-percent reduction in all regional areas in each of 12 patients.

We presumed that single-plane angiograms were capable of tracking an abnormal segment through systole. Although several recent studies argue for biplane angiography to detect otherwise hidden areas of abnormal motion, it is generally held that those aneurysms, which are already identified in the RAO projection, show little or no rotational movement from the single-plane view.

**Figure 2A** (Before nitroglycerin therapy). Superimposed end-diastolic and end-systolic ventricular silhouettes. Dyskinesis of inferior wall is evident, and stippled area represents prolapsed cusp of posterior mitral valve.

**Figure 2B** (After nitroglycerin therapy). Prolapse of mitral cusp is no longer present, and inferior wall no longer expands paradoxically.
Since the initial observation, data have already been presented which support the theory that if treatment with nitroglycerin improves the motion and function of regional areas of ischemia, then bypass of vessels supplying those ischemic zones results in some restoration of contractile function. Our study also suggests that noncontractile ischemic segments are potentially recoverable under different loading states, but in addition it demonstrates that there was an appreciable number of those segments which remained unchanged or worsened in association with nitroglycerin therapy. The identification of the contraction patterns in regional zones of ischemia and the mechanisms underlying their behavior in response to a change in loading state are important fields for further investigation.

References

6 Sniderman AD, Marpole D, Fallen EL: Regional contraction patterns in the normal and ischemic left ventricle in man. Am J Cardiol 31:484-489, 1973
10 Burggraf GW, Parker JO: Left ventricular volume changes after amyl nitrite and nitroglycerin in man as measured by ultrasound. Circulation 49:136-143, 1974
14 Herman MV, Gorlin R: Implications of left ventricular asynergy. Am J Cardiol 23:538-547, 1969
19 McDonald IG: The shape and movements of the human left ventricle during systole. Am J Cardiol 26:221-230, 1970